

UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

In re Bair Hugger Forced Air Warming Products Liability Litigation	MDL No. 15-2666 (JNE/FLN)
This Document Relates to All Actions	EXPERT REPORT OF DR. WILLIAM R. JARVIS

I. Education and Experience

I am a medical doctor with extensive experience in the areas of infectious disease, healthcare epidemiology, infection control, and pediatrics (Attachment A-Curriculum Vitae). I received my M.D. at the University of Texas, Houston in 1974 and my B.S. in Psychology with High Honors at the University of California, Davis in 1970. I was a Pediatrics Intern at the University of Texas at Houston (1974-1975), a Pediatric Resident at the University of Southern California's Children's Hospital of Los Angeles (1975-1977), a Pediatric Infectious Diseases Fellow at University of Toronto's Hospital for Sick Children (1977-1978), a Pediatric Infectious Diseases, Virology and Epidemiology Fellow at Yale University School of Medicine (1978-1980), and an Epidemic Intelligence Service (EIS) Officer and a Preventive Medicine Resident at the Centers for Disease Control and Prevention (CDC) Hospital Infections Program (HIP) (1980-1983).

From 1980-2003, I worked in various leadership roles at the CDC in Atlanta, Georgia, focusing on the investigation and prevention of infectious diseases—particularly infections and other complications associated with healthcare. I held a number of titles during these 23 years, including Assistant Chief, National Nosocomial Infections Surveillance (NNIS) system (currently, the National Healthcare Safety Network [NHSN]); Chief, Epidemiology Branch; Chief, Investigation and Prevention Branch; and Acting Director, Hospital Infections Program (HIP); Assistant Director for Science, Division of Healthcare Quality Promotion (DHQP); and Director, Office of Extramural Research, Office of the Director, National Center for Infectious Diseases. For 17 years, I supervised the conduct of all Divisional outbreak investigations of healthcare associated-infections (HAI) in healthcare settings, the development of HAI prevention guidelines (including the 1999 Guideline for the Prevention of Surgical Site Infections [SSIs]) and of epidemiological studies of HAIs and their prevention.

In addition to my work at CDC, I also was a Clinical Associate Professor at the Emory University School of Medicine and an Assistant Professor at the Emory University Rollins School of Public Health. I am the former president of the Society for Healthcare Epidemiology of American (SHEA) and the former Chair of the Research Foundation of the Association for Professionals in Infection Control and Epidemiology, Inc. (APIC). I have published widely in the areas of infectious diseases, infection control, epidemiology, prevention of SSIs, public health, and pediatrics. I have published >400 peer-reviewed publications, many book chapters and editorials, CDC surveillance reports, and I have edited four books, including the latest

edition of the book Hospital Infections, 6th Edition. Currently, I am a Fellow of the SHEA, the Infectious Diseases Society of America (IDSA), and a member of APIC. I am also the Chairman of the Food and Drug Administration's (FDA's) General Hospital and Personal Use Committee.

I am the recipient of many awards (see Attachment A). Many Public Health Service Awards were for successful investigation of HAI outbreaks. In addition, in 2003, I received the CDC's Lifetime Scientific Achievement Award. This award is given to at most one individual each year. Then, in 2010, I was given the CDC DHQP Lifetime Achievement Award in Epidemiology. That award is given once every 10 years to individuals who have made significant contributions through a lifetime of dedication and productive contributions to infection prevention, healthcare epidemiology, and patient protection.

Since 2003, I have been the President of Jason and Jarvis Associates, LLC. I am responsible for medical consulting in epidemiology, infectious diseases, HAI prevention and control, healthcare epidemiology, protocol design (research), survey/study design and conduct and analysis, and public health. In addition, I provide legal expertise in the areas of healthcare epidemiology, infection control, and infectious diseases.

I have extensive experience in developing HAI surveillance systems and definitions, conducting epidemiological studies and outbreak investigations. My experience that is particularly relevant to this case include: being an author of the CDC HAI definitions—including of the definition of “surgical site infection” (Garner, Horan); being an author of the CDC Guideline for Prevention of Surgical Site Infection (SSI) (Mangram); helping establish the current CDC HAI surveillance system by being Assistant Chief, the NNIS system—the precursor to the current NHSN surveillance system (Jarvis); and being in charge of the HIP/DHQP's HAI epidemiological studies and outbreak investigations.

For approximately 17 years (from 1985-2002), I was responsible for the supervision of all of the CDC HIP's outbreak investigations in healthcare facilities (i.e., inpatient, outpatient, acute care, long-term care, surgicenter, dialysis center, etc.), epidemiological studies of HAIs, and for the development of HAI/infectious diseases prevention guidelines. My experience with investigation of outbreaks in healthcare settings is particularly pertinent and noteworthy. **During this period, I was responsible for more outbreak investigations than anyone else in the world.** Using a systematic approach to these investigations, my team and I investigated >200 on-site investigations and provided guidance on thousands of other outbreaks. Throughout this work, my team and I developed a systematic methodology to investigate infectious disease outbreaks or other complications associated with healthcare delivery. This methodology is centered around a systematic epidemiological-based approach to the investigation of infectious disease outbreaks.

The ultimate goal of each of our investigations was to identify the most likely cause of the outbreak, describe the risk factors associated with the infection/complication, and introduce control measures to prevent the infection/complication from occurring. Two different approaches are commonly used to investigate infectious disease or other HAI outbreaks: 1) the quick and dirty investigation, which often includes conduct of extensive culture surveys to identify the outbreak source or 2) conduct an epidemiological investigation with subsequent epidemiology-directed environmental or personnel cultures or assays (i.e., epidemiological investigation with laboratory confirmation). Experience derived from our team-led investigations throughout the years established that the former “shot-gunning” approach creates

superfluous work and can be counterproductive because risk factors or environmental reservoirs that are epidemiologically relevant might be missed altogether or the wrong (or no) source identified. Using the systematic epidemiological investigation combined with directed cultures/testing led to the identification of the cause of all of the on-site investigations we conducted during my 17 years of supervision of this activity.

Results of these outbreak investigations provide evidence that the epidemiology-directed approach is more accurate, efficient, and less costly for identifying the source and mode of transmission of pathogens and for terminating the outbreak. For certain HIP-conducted outbreak investigations, subsequent laboratory studies indeed confirmed the epidemiological findings. However, my team and I often had to draw conclusions based solely on the epidemiological findings without laboratory confirmation because relevant microbiologic specimens were discarded before the decision to conduct a formal investigation was made. Our team's outbreak investigations established that culture surveys of personnel or the environment without a prior epidemiological investigation can be misdirected, expensive, or a waste of laboratory resources and therefore should not be performed before comparative epidemiological studies are completed. Our team's approach of integrating epidemiology and microbiology remains vital to conducting a successful outbreak investigation. This combined epidemiological-laboratory investigation approach has become the "gold standard" methodology used by others at CDC, DHQP, State Health Departments and by healthcare epidemiologists throughout the world as the best way to investigate outbreaks of infectious or non-infectious complications associated with healthcare delivery. Thus, in researching and preparing this report, I have used this second methodology, the exact same methodology that I used and found effective in my work at the CDC.

Although the basic epidemiological methods used to identify and characterize risk factors associated with HAI outbreaks has remained essentially the same throughout the past 45 years, the overall approach to planning and executing outbreak investigations has evolved substantially. From early on, experience obtained from our HIP/DHQP, CDC team's outbreak investigations demonstrated that, although inadequate infection control practices almost always play a role in transmitting pathogens, HAI outbreaks invariably occur when multiple adverse events (inadvertent or even intentional) go unchecked, occur sequentially, or occur simultaneously. Such events can involve a complex interplay of factors (e.g., unsatisfactory infection control practices by healthcare workers, fluctuating nurse- to-patient ratios and staffing levels, or incorrect device use or sterilization), and these factors have led to the transmission of HAI outbreak pathogens becoming more complicated and difficult to characterize. CDC and other investigators have therefore had to adapt by integrating epidemiology, basic sciences, microbiology, molecular typing, engineering, and advanced statistical methods when conducting HAI outbreak investigations. A testimony to the success of our HIP/DHQP, CDC team's systematic approach is that over the 17 years we identified the source and terminated the outbreak in 100% of the on-site investigations we conducted. For the period 1990-2000, we performed 124 on-site investigations of HAIs or other complications associated with healthcare delivery (Archibald). Almost all of the on-site HAI outbreaks we investigated during this decade or over the 17 years I supervised this activity were published in peer-reviewed publications such as the New England Journal of Medicine, Journal of the American Medical Association, Lancet, the Journal of Infectious Diseases, the SHEA and APIC journals, etc.

In addition to my experience investigating HAI outbreaks, I have extensive experience developing HAI surveillance definitions and designing HAI surveillance systems (Garner, Horan, Jarvis). I was involved in the development of the CDC definitions of SSI and was an author of the papers outlining these definitions (Garner, Jarvis). I have extensive experience in the identification of SSIs using interpretation of clinical and/or laboratory findings, both through the surveillance system, in epidemiological studies and through outbreak investigations. It is crucial that surveillance systems, epidemiological studies, and outbreak investigations use SSI definitions that are consistent and standardized; otherwise, inaccurate or uninterpretable SSI rates will be computed and reported. During my tenure at the CDC, we, through the CDC's HAI surveillance system using a systematic approach, developed standardized surveillance criteria for defining SSIs (Figure 1). By these criteria, SSIs are classified as being either incisional or organ/space (Garner, Horan). Incisional SSIs are further divided into those involving only skin and subcutaneous tissue (superficial incisional SSI) and those involving deeper soft tissues of the incision (deep incisional SSI). Organ/space SSIs involve any part of the anatomy (e.g., organ or space), other than incised body wall layers, that was opened or manipulated during an operation.

Currently, as President of Jason and Jarvis Associates, LLC, I consult on prevention of HAIs and infectious diseases throughout the world. I consult for individual hospitals, hospital systems, CDC, Ministries of Health, national and international infection control societies, medical device and product manufacturers, and serve as a medical expert in legal cases (Attachment B--see attached list of cases in which I have provided a deposition or trial testimony). I have provided depositions or trial testimony regarding a number of infectious diseases issues and have been accepted as a medical expert in these cases without exception. I continue to use the same, scientifically rigorous and generally accepted systematic investigative approach I used while I was at the CDC. My fee schedule, which sets forth my compensation for work as an expert witness, is attached hereto as Attachment C.

II. Basic Microbiology, Infectious disease, and Sources of Prosthetic Joint Infections

The risk of an SSI occurring is dependent upon three factors: 1) the pathogen; 2) the patient, and 3) the mode of transmission. No SSI will occur, regardless of the patients' risk factors, if a pathogen is not present at the site. Although theoretically any pathogen gaining access to the surgical site can cause an SSI, the most common pathogens causing SSIs are bacteria, specifically *Staphylococcus aureus* (30.0%), Coagulase-negative staphylococci (CNS; 13.7%), *Enterococcus* spp. (11.2%), *Escherichia coli* (9.6%), or *Pseudomonas aeruginosa* (5.6%) (Hidron 2008, Hidron 2009). *S. aureus* and CNS are common organisms found on the skin of humans. Each of these and other infecting pathogens can arise from an endogenous or exogenous source. Endogenous sources include the patients' own flora—from their skin, mucous membranes, gastrointestinal tract, or seeding from a distant focus of infection. Exogenous sources include: (1) the surgical personnel (surgeon and team) through their soiled attire, breaks in aseptic technique, or inadequate hand hygiene; (2) the operating room (OR) physical environment and ventilation; or (3) tools, equipment, machines, or other materials brought to the OR or into the operative field.

Patients have a wide variety of risk factors that can increase the risk of an SSI if a pathogen contaminates the surgical site. These risk factors can include: age (i.e., old and very young), diabetes, nicotine use, steroid use, malnutrition, obesity, prolonged pre-operative stay,

pre-operative nares colonization with *Staphylococcus aureus*, infections at a remote body site, being immunocompromised, etc. Again, it should be emphasized that none of these patient-specific characteristics causes the infection; the pathogen causes the infection. These patient risk factors just increase or decrease the risk of infection if a pathogen contaminates the surgical site.

Last is the mode of transmission. Exogenous sources account for the majority of SSIs. Surgical personnel, instruments, equipment and the OR environment can be the source of the pathogen. Transmission can be through direct contact (i.e., hand or intrinsically contaminated instrument/solution touches the surgical site) or via indirect contact (contaminated air or extrinsically contaminated hand or instrument/solution contacts the surgical site). Many interventions are made to reduce the risk associated with these exogenous sources. They include: (1) instrument/solution sterilization; (2) requiring OR personnel to perform extended hand hygiene and wear appropriate clothing to protect the patient from surgical staff flora (i.e., gowns, gloves, face masks, hats, etc.); and (3) minimizing the number and movement of surgical personnel and their entry/exit from the specially ventilated OR. Each person sheds approximately 10^9 skin squames daily; 10% are <10 μm and each skin squame is capable of carrying four bacteria. For this reason, the number and movement of personnel is minimized and the OR heating ventilation and air conditioning (HVAC) system is optimized with high efficiency particulate air (HEPA) filtration, 20-25 air changes per hour, appropriate air temperature and humidity, and in some instances directional or laminar air flow to reduce the risk of airborne contamination of the surgical field. All of these measures to reduce the risk of pathogen transmission are critical, particularly in prosthetic joint arthroscopy (PJA) procedures, as the implant can provide a nidus for bacterial adherence. Bacterial colonization can lead to biofilm formation, a proteinaceous covering, which protects the bacteria from antimicrobial therapy and the patient's immune system. Thus, PJA SSIs can be very difficult to treat and the implant must often be removed for successful antimicrobial treatment.

There are various primary and secondary sources of bacteria that can lead to prosthetic joint infections (PJIs). The primary reservoirs of bacteria in the room are the people, that is, the OR staff and the patient (Whyte 1988). The concentration of bacteria in the OR air is proportional to the number of people and their activity (Lidwell, 1967; Hambræus) and it is therefore the surgical team, rather than the patient, who disperse most of the airborne bacteria. (Whyte 1988). It is well known that the surgical personnel in the OR shed skin squames and can increase airborne bacterial concentrations in the OR. In one study (Whyte 1976), a person wearing a cotton suit commonly used in the OR released a median number of 1,338 bacterial particles per minute into the OR air. In another study (Suzuki), the particle counts increased from 1.1 to 42.5 colony forming units (CFUs)/ m^2/min (39 times increase) measured by split sampler and from 1.5 to 17.4 CFU/ m^2/min (12 times increase) in an empty vs. in-use OR. Organisms released by OR personnel vary widely by type and amount, but can include CNS, *S. aureus*, *Haemophilus influenzae*, *Neisseria meningitidis*, or *Streptococcus pyogenes* (Group A Streptococcus or GAS). Importantly, these particles generally fall or settle quickly and contaminate the environment (especially on the floor).

Secondary sources of pathogens that can get to the sterile wound and result in PJIs are from equipment/devices which can become contaminated with bacteria from the primary reservoirs (Whyte 1988). A recent vivid illustration of this is the worldwide outbreaks of *Mycobacterium chimaera* SSIs following cardiac surgery that have been linked to heater-cooler units (HCUs), which will be discussed in more detail in Part VII, below. ***The infections***

associated with HCUs are the result of contaminated exhaust air causing contamination of the OR air and specifically the “sterile” surgical site in cardiac surgery patients. Following several investigations documenting the mechanism of these SSIs, the CDC and their Healthcare Infection Control Practices Advisory Committee (HICPAC) have expressed strong concern about any air blowing devices in the OR. HICPAC has therefore recommended that “nothing that blows air should be in an operating theater, if possible” (CDC-A, B, C). The Bair Hugger FAW is a similar type of secondary reservoir in that it uses non-sterile air in its air intake and then further contaminates that air within the device, which it subsequently exhausts into the blanket near the “sterile” surgical field.

III. Surgical Site Infections

According to the CDC, in 2006, ~80 million surgical procedures were performed in U.S. inpatient and outpatient/ambulatory care settings (Berrios-Torres). Between 2006 and 2009, SSIs complicated ~1.9% of all surgical procedures performed in the United States. This estimated number of SSIs is likely an underestimate, since ~50% of these SSIs only become evident after healthcare setting discharge. From January 2009 through December 2010, SSIs accounted for 23% of the 69,475 HAIs reported by 2,039 hospitals to CDC’s National HAI surveillance system—NHSN (Berrios-Torres). Variations in the surveillance definition of an SSI, combined with inconsistencies in diagnostic related group (DRG) coding, and variations in post-discharge SSI surveillance, makes it difficult to evaluate or compare interventions and track secular trends in SSI rates.

The identification of an SSI involves interpretation of clinical and laboratory findings, and it is crucial that a surveillance program use definitions that are consistent and standardized; otherwise, inaccurate or uninterpretable SSI rates will be computed and reported. During my tenure at the CDC, we, through the CDC’s HAI surveillance system, developed standardized definitions for SSIs (Figure 1) and standardized surveillance protocols for detecting and reporting SSIs (Garner, Horan).

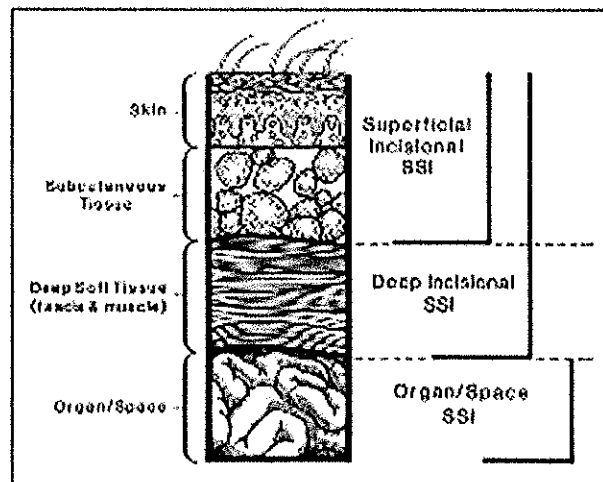


Figure 1. Cross-section of abdominal wall depicting CDC classifications of surgical site infection.

By these criteria, SSIs are classified as being either incisional or organ/space. Incisional SSIs are further divided into those involving only the skin and subcutaneous tissue (i.e.,

superficial incisional SSI) or those involving deeper soft tissues of the incision (i.e., deep incisional SSI). Organ/space SSIs involve any part of the anatomy (e.g., organ or space), other than incised body wall layers, that was opened or manipulated during an operation.

SSIs result in increased morbidity, mortality, and direct and indirect costs including increased hospital length of stay, readmission, repeat surgical procedures, outpatient/emergency room visits, additional medications (i.e., antimicrobials), lost productivity, temporary or permanent disability, and even death. Actual attributable costs of SSIs are difficult to determine. SSIs are very costly to the patient, the hospital, and the healthcare system. Estimated average attributable SSI costs range from \$10,443 to \$25,546 per infection. However, the costs of PJIs can exceed \$90,000. The most common pathogens causing SSIs are common human skin organisms—*S. aureus* and CNS, but infecting pathogens can vary by site of the procedure.

Risk factors for SSIs include both patient-related (i.e., co-morbidities) and procedure-related factors. Patient-related risk factors include: age, gender, weight (obesity), underlying diseases (i.e., diabetes, immunosuppression), etc. Procedure-related factors include patient skin preparation, duration of the procedure, surgical technique, OR personnel, and air handling/ventilation, etc. Although there are overall general SSI risk factors, numerous studies have shown that there are also procedure-related risk factors (i.e., vascular vs. cardiac vs. orthopedic procedures) (see discussion of prosthetic joint procedure SSI epidemiology and risk factors below). As discussed below, a large number of pre-operative, intra-operative, and even post-operative interventions are implemented to reduce or eliminate these SSIs. It should be emphasized that these risk factors do not cause a SSI or PJI. **For a SSI/PJI to occur, contamination of the wound must occur.** The risk factors just increase/decrease the likelihood that an infection will occur if such contamination occurs.

A wide variety of interventions are implemented to reduce the risk for an SSI. In order to cause an SSI, pathogens--usually bacteria--must enter the surgical wound. These bacteria can arise from a variety of sources including the patients' own skin flora, skin flora of OR personnel, contaminated equipment, solutions, or personnel protective equipment in the OR, or OR air. Thus, a variety of interventions or SSI Prevention Bundles of evidence-based practices have been developed and implemented. These include interventions aimed at the patient, the OR environment, OR equipment, and the OR healthcare personnel practices.

To reduce the risk of infection associated with the OR environment and equipment a number of interventions are implemented. Special handling (i.e., HEPA or other filtration) of the air entering the OR reduces the microbial flora in the air (in high risk prosthetic joint procedures some even use directional or laminar air flow to further reduce OR-contaminated air from circulating into the operative field). Keeping the OR doors closed and reducing/minimizing the number of surgical personnel in the OR and the frequency of entry/exiting of personnel reduces the microbial flora that these personnel disperse into the environment/air and reduce air from outside the OR from entering and mixing with OR filtered air. Insuring appropriate sterilization of equipment, instruments, solutions, etc. having potential contact with the surgical field reduces the risk of external contamination of the operative wound. Minimizing the equipment in the OR that is outside the operative field and ensuring that exhaust from such equipment does not impact the operative sterile field reduces the risk of contaminated air or fluids entering the operative field and contaminating the surgical wound. Appropriate cleaning of the OR between procedures

and at the end of the day, reduces the microbial contamination of walls, floors, surfaces and equipment in the OR.

Healthcare (OR) personnel practices to reduce the risk of SSI include appropriate pre-operative hand hygiene, wearing appropriate sterile personnel protective equipment (i.e., gowns, gloves, masks, hoods), reducing the number and movement of OR personnel, insuring good surgical technique, shorter duration of the procedure, and proper hemostasis. The OR staff interventions are implemented to reduce the microbial burden on OR personnel, decrease the dispersal of OR personnel skin flora, and thereby reduce surgical field/wound potential contamination in the OR.

Data from the CDC's NHSN have demonstrated that surgical-procedure specific and surgeon-specific SSI rates are essential. One cannot generalize from one surgical procedure (i.e., cardiac or general surgery) to another (orthopedic or specifically to total knee arthroplasty [TKA] or total hip arthroplasty [THA] procedures). The CDC's NHSN collects data for general risk factors for an SSI (i.e., procedure, wound class, duration of the procedure, and severity of illness of the patient measured by American Society of Anesthesiologists [ASA]). However, this risk index does not predict SSI risk very well for homogenous procedures—such as TKAs or THAs. Furthermore, procedure-specific risk factors, defined by peer-reviewed studies, are not collected in the CDC NHSN surveillance system.

Studies of the epidemiology of SSIs have documented that a large number of evidence-based preventive interventions aimed at the patient, OR environment/equipment, and OR personnel can be implemented and markedly reduce the risk of an SSI occurring after a surgical procedure.

IV. Peer-Review Literature Demonstrating Problems with the Bair Hugger

When considering the potential risk to patient safety posed by a medical device, it is helpful to review the experimental evidence which has appeared in clinical peer-reviewed publications over the years. In doing so, I have reviewed a significant amount of peer-reviewed published scientific material which supports the conclusion that the Bair Hugger Forced Air Warmers (FAWs) have: inadequate air filtration efficiency, internal bacterial contamination (including intake and exhaust hoses), exhaust microbial contaminants, interfere with OR airflow (directional or non-directional), and can introduce particles/microbial contaminants into the surgical “sterile” field.

Several of the studies discussed below have documented that the Bair Hugger FAW intake air filter does not adequately filter the air (unlike a HEPA filter would do), that the internal device and intake and exhaust hoses become bacterially contaminated, and that the hoses exhaust contaminated air.

Each of the Bair Hugger models has an air intake on the bottom of the device. Thus, the ambient air withdrawn into the device is from the non-sterile floor area (some devices can be elevated and obtain their air from the non-sterile ambient air above the floor). This air passes through (and reportedly around) a filter, is heated in the device (when on), and is exhausted through an output hose and through a blanket onto the surgical patient. Given this design, how might the Bair Hugger FAW impact the OR air and environment?

First, the air pulled into the Bair Hugger FAW device is non-sterile ambient air from below the OR table, and often directly from the floor area. Published literature (Albrecht 2010) and experts' reports (e.g., Dr. David's report) have found that 3M chose to drastically decrease the filtration efficiency on Bair Hugger FAWs. The fact that these devices do not use a HEPA filter concerns me because, as illustrated by a number of studies, the devices then exhaust bacterially-contaminated air into the area of the surgical field. This adds support to my opinion that use of the Bair Hugger increases the bacterial load reaching the surgical site.

For example:

- Albrecht et al. showed that 58% of the FAWs tested were internally generating and emitting airborne contaminants with microorganisms detected on the internal air path surfaces in 92.3% of these blowers. Isolates of *Staphylococcus aureus* (13.5%), CNS (3.9%) and methicillin-resistant *S. aureus* (MRSA; 1.9%) were detected in the FAW blowers (Albrecht 2011).
- Reed et al. documented that the intake air filtration of the Bair Hugger model 750 was found to be 63.8%. In this study, cultures from 100% of the FAWs were positive; CNS, mold and micrococci were identified. Particle counting showed that 96% of the FAWs were emitting "significant levels" of internally generated airborne contaminants out of the hose end (Reed).
- Avidan et al. tested nine Bair Hugger and one Warm Touch FAWs. Agar plates placed directly in the air stream grew pathogenic organisms from four of the units (3/4 were Bair Hugger FAWs). Organisms recovered include CNS, *Corynebacterium* spp., *Aspergillus fumigatus*, and *Cryptococcus albidus*. Sites swabbed that were culture positive were from the outside of the filter, proximal hose, and the distal hose. (Avidan).
- Albrecht et al. cultured 25 in-use Bair Hugger FAWs and found that 24% of the FAWs blowers were emitting significant levels of internally generated airborne contamination in the 0.5 to 5.0 micron size. Microorganisms were detected in the internal air pathways of 94% of the blowers. (Albrecht 2009).

These studies show that the Bair Hugger filter efficiency is much lower than indicated, that the intake hose, internal units, and output hose can be culture positive with pathogenic organisms, and that air blown through these devices can produce contaminated air. Operating instructions from the Bair Hugger manufacturer do not provide a method for decontaminating the inside of the hose or blower.

A number of studies have assessed the impact of the Bair Hugger FAWs on OR air particulate counts and/or microbial CFUs.

- Albrecht et al. measured the emission of viable and non-viable airborne contaminants of the FAW blowers (Albrecht 2009). They found that Bair Hugger blower surfaces were contaminated with pathogens and that they blow a large number of particles into the sterile field.

- Albrecht et al. also assessed the filter efficiency of Bair Hugger 505, model 200708D and model 200708C 0.2 micron intake filters obtained from the manufacturer (Albrecht 2011). They found that the intake filter retention efficiency at 0.2 microns was 93.8% for the 200708C filter and 61.3 % for the 200708D filter. Fifty-eight percent of the Bair Hugger blowers were internally generating and emitting airborne contaminants, with microorganisms detected on the internal air path surfaces of 92.3% of the blowers. *S. aureus*, CNS, and MRSA were detected in 13.5%, 3.9% and 1.9% of the Bair Hugger blowers, respectively. These authors found that an inadequate filter was allowing microbes into the Bair Hugger and also detected re-introduction of these contaminants into the blower air stream. They concluded that “the design of popular FAW devices using the 200708C filter was found to be inadequate for preventing the internal buildup and emission of microbial contaminants into the operating room.”
- Reed et al. assessed the efficiency of the intake filters of Bair Hugger model 750 and found the intake filter to be 63.8% efficient (Reed). Swabbing detected microorganisms within 100% of the Bair Hugger blowers. Distal hose end air stream particle emissions were well above what would be expected based on intake filter performance; 96% of the Bair Hugger blowers were emitting significant levels of internally generated airborne contaminants out of the exhaust hose end and they calculated that 82,500 particles per second were being emitted from the Bair Hugger hose ends. When the 23 Bair Hugger FAW blowers were tested in an OR, they were found to generate particulate counts ranging from 150 to 39,000 (median 4,400) particles >0.3 micron/cu ft. These authors concluded that there was a “need for upgraded intake filtration, preferable high-efficiency particulate air filtration (99.97%) . . . to reduce contamination buildup and emission risks.”

These studies document that the Bair Hugger FAW filters are inadequate and that this leads to internal machine and intake and exhaust hose contamination with potential pathogens that are then released out the exhaust hose leading to both particulate and pathogen contamination of the sterile surgical field.

Others have assessed the impact of Bair Hugger FAWs on OR air or ventilation performance.

- McGovern et al. used neutral-buoyancy detergent bubbles released adjacent to a mannequin’s head and at the floor level to assess particulate and air currents during a simulated hip replacement in an OR (McGovern). Bubble counts over the surgical site were greater when Bair Hugger FAWs (models 540 and 525) were used compared to conductive fabric warming. Bair Hugger FAWs generated convection currents that mobilized floor air into the surgical site area.
- Legg et al. assessed the impact of Bair Hugger FAWs on the temperature and particles over a simulated lower limb arthroplasty procedure with a human volunteer (Legg 2012). They found that the Bair Hugger FAW significantly increased the temperature (1.1°C vs 0.4°C, $p < 0.0001$) and the number of particles (1,038.2 vs 274.8, $p = 0.087$) over the surgical site compared to radiant warming.

- Dasari et al. assessed whether the floor-to-ceiling temperatures around a draped mannequin in a laminar-flow theatre differed with a Bair Hugger FAW (Model 525) blanket, an over-body convective blanket, or an under-body resistive mattress (Dasari). With the Bair Hugger FAW, the mean temperatures were significantly elevated over the surgical site vs. the other technologies. The authors concluded that Bair Hugger FAWs “generates convection current activity in the vicinity of the surgical site.”
- Belani et al. assessed the release of neutral-buoyancy detergent bubbles in the head-side region of the anesthesia drape (low vs. high) of an OR with downward displacement used for orthopedic surgery and tracked the bubbles when Bair Hugger FAW (model 540), conductive fabric, or no device was used (Belani). They found that the direct mass-flow exhaust from the Bair Hugger FAW generated hot air convective currents that mobilized significantly more bubbles (average: 132.5 FAW vs. 0.48 conductive fabric [$p = 0.003$] vs. 0.01 for control conditions [$p = 0.008$]) across both drape heights. The authors concluded that excess heat from forced air warming resulted in the disruption of ventilation airflows over the surgical site.
- Legg et al. used neutral-buoyancy helium bubbles and particles created using a Rocket PS23 smoke machine positioned below the OR table to demonstrate the impact of the excessive heat from FAWs (Legg 2013). They used the same OR, devices, and controls as previously used (Legg 2012). The Bair Hugger FAW waste heat increased the air temperature on the surgical site of the drape by $>5^{\circ}\text{C}$. The convection currents rose against the downward unidirectional airflow causing turbulence over the patient and increased particle concentrations by 2000-fold (2,174,000 particles/ m^3 for Bair Hugger FAW vs. 1,000 particles/ m^3 for radiant warming and 2,000 particles/ m^3 for controls) by drawing potentially contaminated particles from below the OR table into the surgical site.
- Sessler et al. evaluated the air quality in laminar air flow ORs at two hospitals using a “volunteer patient and heated mannequin surgeons” by assessing tracer background particle counts near the putative surgical site with a FAW blower (Bair Hugger model 522 and 635) set off, blowing ambient air, and blowing warm air (Sessler). The mean particle counts were higher at both institutions when the Bair Hugger FAW was on vs. off (mean 6.7 vs 9.0/9.4 and 26 vs 161.9/102.6).
- Dr. Elghobashi, using high-fidelity, large-eddy simulation (LES) to assess the interaction of the OR ultraclean ventilation air flow and the flow created by the Bair Hugger FAWs found that the Bair Hugger FAW hot air generated forced convective currents and strong thermal plumes that disrupted the directional clean air ventilation and produced large levels of turbulence under the operating table bringing contaminants from the floor area into the “sterile” surgical field (Dr. Elghobashi report).

Thus, these studies document that Bair Hugger FAWs generate excess heat that disrupts OR air (directional or non-directional) and produce convection currents that can circulate contaminants via the airborne route from the floor or other areas into the area of the sterile surgical field.

In addition, there are a number of publications linking Bair Hugger FAWs with infections.

- Bernards et al. investigated two outbreaks of multidrug-resistant *Acinetobacter baumannii* in their intensive care unit (ICU) (Bernards). They identified the Bair Hugger FAW as one of the medical devices that were involved in the outbreaks. They reported that they “found contaminated dust in the interior of different types of machines used by patients.” They also reported that “The Bair Hugger is designed to create an airflow; dust is sucked into the machine, with filters becoming contaminated and possibly serving as a secondary source of transmission.” After the removal of the dust and replacement of the filters of the Bair Hugger FAW, the first outbreak was stopped. This study demonstrates the critical function of the filter and its maintenance in preventing the compromise of patients’ clean environment protection in the operating theater.
- McGovern et al. evaluated the SSI risk with hip and knee replacement surgeries and found an increased SSI rate (Odds Ratio = 3.8, $p = 0.024$) during a period when FAWs were used compared to when conductive fabric warming was used (McGovern).
- Wood et al. reviewed the published experimental and clinical research into the issue of the Bair Hugger’s infection risk (Wood). In light of the hazards raised by the product, the authors recommended that facilities explore the use of alternative warming technologies in ultraclean orthopedic procedures.

These studies document that the SSI risk associated with Bair Hugger FAWs is not just theoretical, based upon studies showing that: 1) the device intake air is not sterile; 2) the device intake air filter is not HEPA-filtered and the filter used has been shown to be inadequate to filter out bacterial contaminants; 3) studies have shown that the internal device and intake and exhaust hoses (and the air they exhaust) are contaminated; 4) the air exhausted from the device has high particulate counts and bacterial CFUs—i.e., it is contaminated; 5) the exhaust air and excess heat both lead to particulate and airborne bacterial contamination of the sterile surgical field; and 6) particulate and bacterial contamination of the sterile surgical field can lead to infection.

Some have argued that even if the Bair Hugger FAW air output/exhaust to the blanket is bacterially contaminated, as documented in many studies above, the blanket itself would serve as a secondary method of filtration to prevent these contaminants from reaching the surgical site. There are no data to substantiate this claim. Furthermore, there are data to show that this is not correct. First, the studies above used the Bair Hugger FAWs with the exhaust hose connected to the blanket (and in normal use) and still found elevated particle counts and CFU in the OR air and near the “sterile” operative field. Second, a meeting presentation from M.D. Anderson Cancer Hospital in Houston, Texas clearly showed there is no secondary filtering when their Bair Hugger FAW inadvertently became wet in the OR during a patient’s surgical procedure (Tsai). The engine inside the machine began to burn and the resulting electrical burning soot was blown from inside the Bair Hugger FAW, through the exhaust hose, and then through the blanket to the patient. Evidence of this soot being transferred from the Bair Hugger FAW internal engine to the patient was illustrated by the soot marks pictured on the skin of the patient in the pattern of the Bair Hugger blanket holes. Thus, there are data to visually illustrate that the Bair Hugger FAW blankets are not secondary filters of the exhausted air.

These studies provide substantial evidence of the patient safety risk posed by the Bair Hugger FAWs. While the individual results of these studies are not definitive, collectively they firmly support the following contentions:

1. Bair Hugger FAW machines inadequately filter non-sterile ambient air;
2. Bair Hugger FAW internal surfaces (i.e., machine, intake, and exhaust filters) become contaminated by microbes from the ambient air in the OR;
3. Bair Hugger FAWs exhaust this contaminated air into the OR/sterile surgical field through the exhaust hose and the blanket;
4. Bair Hugger FAWs markedly increase the bioburden (i.e., particulates and CFUs) of the OR directly (via exhaust air) and indirectly by disruption of OR air ventilation (directional or non-directional) through the excess heat produced; and
5. Bair Hugger FAWs promote circulation of microbial contaminants into the “sterile” surgical field.

I have also reviewed literature that has been promoted by the Defendant as supporting the safety of FAWs in orthopedic surgical procedures. However, these studies are not convincing on this issue.

- Zink et al. studied eight volunteers who lay on an OR table with their lower bodies and legs covered with a warming cover and sterile drape (Zink). Convection warming was administered for two hours and then no warming for two hours. Culture plates were placed directly on the volunteers’ abdomens through an opening in the drape. This study appears to have used new uncontaminated blowers and it was not conducted under actual surgical conditions. In light of the date of the study, the test appears to have been conducted with Bair Hugger Model 500 series units with lowered airflow and the original filter instead of the reduced efficiency model. It does not appear that any surgeons, other OR staff, equipment or any flow obstructions were in the room. Despite this, they still detected bacterial contamination on 2/8 (25%) of the culture plates.
- Huang et al. analyzed air and wound cultures for bacterial content at the beginning and end of surgery from 16 patients undergoing abdominal vascular prosthetic graft insertion procedures (Huang). The study was underpowered to detect a difference in SSIs, did not involve orthopedic surgical patients, was not a controlled study, and was not conducted in OR with directional or laminar flow ventilation.
- Moretti et al. studied the bacterial contamination of air in the OR during 30 female patients (20 with use of the Bair Hugger FAW) undergoing non-cemented hip implantations using an Active Surface Air (SAS) sampler and a single culture plate (Moretti). The study was not randomized, it was not conducted in an OR with directional or laminar flow ventilation, and used a less sensitive air sampler. Despite these limitations, the study still did document an increase in mean bacterial load values when the Bair Hugger FAW was employed. The sample size was too small to detect a difference in SSI risk and the authors concluded that “further studies are needed.”

- Sessler et al. evaluated air quality in two hospital's laminar air flow ORs using a volunteer "patient" and heated mannequin "surgeons" (Sessler). This study was sponsored by and the publication edited before journal submission by the Defendant. Neither Dr. Sessler nor Mr. Olmstead (first and second authors on the study) was involved in the design of the study, and they were not at the hospitals in Holland when the study was performed, and were not involved in the initial analysis of the data. Nevertheless, this study did find elevated particle counts when the Bair Hugger FAWs were on with either blowing of ambient air or warmed air vs. no FAW use. The mean particle counts with the Bair Hugger 522 model were: 6.70 when off vs. 9.00 when on ambient vs. 9.40 when on warm. The mean bacterial counts for the Bair Hugger model 635 were 26 when off vs. 161.90 when on-ambient vs. 102.60 when on-warm.
- Dr. Elghobashi performed high-fidelity, large-eddy simulation (LES) to study the interaction of the OR ultraclean ventilation air flow and the flow created by the Bair Hugger FAWs. He used a full three dimensional design of an OR with an operating room table, surgical lamps, surgical staff, side tables, a FAW and a patient undergoing knee surgery. Two computation models were performed with the blower-off and the blower-on. The FAW hot air generated forced convective currents and strong thermal plumes that interacted with the clean air ventilation. He placed 3 million squames (10 micron diameter) on the floor in a small region surrounding the operating table and surgeons. When the FAW blower was on there was significantly modified and large levels of turbulence intensity observed under the operating table. The turbulence intensity levels were as high as 60% in regions affected by the rising thermal plumes from the blower. Drastic differences were seen in the trajectories of the squames when the blower was off vs. on. When the blower was off, the majority of squames were dispersed by the ventilation towards the outlet grills. None of the squames rose to the level of either the side tables or the operating table. In contrast, when the blower was on, large numbers of squames were lifted upwards by the thermal plumes. Some of the squames were lifted above the surgeons' heads and blown towards the operating table. Large numbers of squames were seen surrounding the surgeons' hands, above the side table, and even very close to the patient's knee or surgical site.

In summary, the above data illustrate that: 1) the Bair Hugger intake air filtration is inadequate; 2) the internal device and the intake and exhaust air hoses become contaminated with bacteria; 3) the exhaust hose is directing bacterially contaminated air to the blanket; 4) the exhausted contaminated air and the disruption is not "secondarily filtered" by the blanket and can reach and contaminate the sterile surgical site; and 5) the excess heat produced by the Bair Hugger FAW disrupts the OR air (directional or non-directional) and leads to particulate and bacterial (i.e., CFU) contamination of the "sterile" surgical site. These data are critical in showing that the Bair Hugger FAWs can lead to surgical field contamination and SSIs.

V. Particle and Microbial Counts in Operating Rooms and the Impact of Reduced Air Quality in Joint Surgeries

A. Airborne Particulates and CFU's:

Using sampling technologies to assess the ambient air in ORs, studies have documented the widespread presence of airborne particulates and microorganisms during surgery.

- Stocks et al used a standard particle analyzer to measure the number and diameter of airborne particulates and an impact air sampler and standard culture plates to identify and count CFU during 22 joint arthroplasty surgeries (Stocks). Particulate density averaged $>500,000$ particles/m³ per 10-minute interval and 1,786 CFU were identified, primarily gram-positive cocci. Particle and CFU density increased with longer surgery duration and higher OR staff counts.
- Edmiston et al. performed in situ air-sampling analysis of multiple distances, ranging from 0.5m to 4m, from the surgical wound in the OR (Edmiston 1999, 2005). CNS were recovered from 86% of air samples, 51% from within 0.5 m of the surgical wound, whereas *S.aureus* was recovered from 64% of air samples, 39% within 0.5 m from the wound. When anterior nares swabs were obtained from 11 members of the operative team, clonality was documented between eight strains of *S. epidermidis*, and 2 strains of *S. aureus* collected from the OR staff and the environment.
- Lidwell et al. found a correlation between the mean values of air contamination and the numbers of bacteria isolated from orthopedic surgical wound wash-out samples (Lidwell 1983). They concluded “that by far the largest proportion of bacteria found in the wound after the prosthesis had been inserted reached it by the airborne route.”
- Andersson et al. assessed the impact of OR traffic patterns on particle counts and CFUs using active air sampling and observations during 30 orthopedic procedures (Andersson). Their data showed a strongly positive correlation between the total CFU/m³ per operation and total traffic flow per operation ($r = 0.74$; $P = .001$), even after controlling for duration of surgery. There also was a positive correlation between CFU/m³ and the number of persons present in the OR ($r = 0.22$; $P = .04$). Traffic flow, number of persons present in the OR, and duration of surgery explained 68% of the variance in total CFU/m³ ($P = 0.001$).
- Darouiche et al. assessed the airborne microorganism CFU at the surgical incision and the impact of using an air barrier system (i.e., intervention) that would reduce particle counts and CFUs at the incision site in total hip arthroplasty, spinal fusion, and vascular surgery patients (Darouiche). They found that the CFU density at the incision site was significantly lower in the intervention group, that the airborne CFU densities were significantly related to the incidence of implant infection, and that the only implant infections that occurred were in the non-intervention group with the higher CFU densities.

Cumulatively, these studies show that airborne particle counts and microbial CFUs can be elevated near or at the operative/incision site and that activities that increase the particle counts/microbial CFUs increase the risk of SSI.

B. *Why Implant/Device Surgeries are Different:*

These and other data show that there are two primary modes of transmission of pathogens causing SSIs. These include direct and indirect contact. Direct contact would involve person to person contact transmission to the surgical site. In contrast, indirect transmission results from contamination of equipment, instruments, solutions, or air that subsequently contaminates the surgical site.

For SSIs, the OR air bacterial load is critically important, as the patients' "sterile" surgical field and surgical site has exposure to this air during the entire length of the surgical procedure. This is particularly important in PJA procedures where an implant is introduced. It has been estimated that rather than large numbers of micro-organisms required to cause many infections, that as few as 1-10 CFUs are required to cause a PJI. Whyte et al. showed that the average air counts in a conventionally ventilated OR was 413 cfu/m³, but in an adjacent ultraclean OR it was 4 cfu/m³, a 100-fold drop from one OR to the other (Whyte 1988). When the wound was washed out just before closure an average of 105 bacteria was found in the wounds in the conventional OR and 3 bacteria in the ultraclean—a 35-fold drop. They calculated that in the conventionally ventilated OR 98% of the wound bacteria came from the air."

It is for these reasons that CDC and national and international Surgical and OR Environmental Societies have recommended: 1) 20 air exchanges per hour and/or use of directional air flow; 2) minimizing the number of OR personnel, their entry and exit of the OR, and their activities; and 3) "Nothing that blows air should be in an operating theater, if possible". (CDC-A, B, and C). Hospitals spend large amounts of money to design and maintain OR HVAC systems to reduce the microbial burden in the OR air.

The primary portal of entry for pathogens causing PJIs is during the surgical procedure when the wound is open to direct contact (personnel and equipment/instruments) and to the OR air. In order to cause a PJI, pathogens—usually bacteria—must enter the surgical wound. Since in most PJA procedures, the joint/surgical wound is closed at the end of the surgical procedure, contamination of the wound/joint/prosthesis can only happen peri-operatively when the implant and joint space are open and exposed. The previously mentioned studies have shown that the particle counts and CFUs in the OR air increase when the number of personnel increase, OR personnel enter and exit the OR (mixing non-OR air with the filtered OR air), equipment, such as the Bair Hugger FAW, exhaust bacterially contaminated air into the OR, and that the excess heat produced by the Bair Hugger FAW can circulate microbial contaminants below the OR table into the "sterile" surgical field. Such contaminated OR air can contaminate surgical gloves, surgical instruments, implants, and the surgical wound.

PJA patients are extremely susceptible to PJIs. This primarily results not from their underlying conditions, which can contribute to their SSI risk, but because they are having a prosthetic device implanted.

- Foster & Hutt (1960) found that experimental septic skin lesions could be produced by as few as 15 organisms (Foster).
- Whyte et al. have said that: "orthopaedic implant operations are susceptible to a lower dose of a less pathogenic bacteria than many other operations." (Whyte 1988).
- It would appear that in orthopedic implant surgery wound sepsis, the infection may be produced by fewer organisms, even a single *S. aureus* (Lidwell 1983, Whyte 1988).

Any indwelling medical device or prosthetic implant has the potential to become colonized by organisms embedded in biofilm. A biofilm is defined as a sessile community characterized by cells that are irreversibly attached to a substratum or interface or to each other, are embedded in a matrix of extracellular polymeric substances that they have produced, and

exhibit an altered phenotype with respect to growth rate and gene transcription. Biofilm organisms exhibit significant resistance to antimicrobial agents (10 to 1,000 times the minimum inhibitory concentration [MIC]) compared to their free-floating, planktonic counterparts. Mechanisms associated with this increased antimicrobial resistance include delayed or decreased penetration of the antimicrobial through the biofilm matrix, altered growth rate of the biofilm organisms, and/or other physiologic changes due to the biofilm mode of growth. Each year in the United States, approximately 13 million patients experience a biofilm-related infection associated with prosthetic implants or invasive devices.

- Susceptible hosts who are exposed to pathogens during a PJA procedure have different periods of latency (i.e., time from inoculation to signs of infection) before the manifestation of symptoms of infection because such small CFUs of pathogens are necessary to cause the infection and because of the fact that such organisms commonly attach to the prosthetic device, which has no blood supply, and thus the organisms can grow slowly. According to the CDC SSI definitions, any SSI developing in a PJA procedure patient can present within one year. However, the recent HCU outbreaks of *M. chimaera* have shown that the latency period can be measured in years (Chand, Haller, Kohler, Perkins, Robinson, Sax, Soetaert, Sommerstein, and Trudzinski).
- Risk factors for SSIs include both patient-related (i.e., co-morbidities) and procedure-related factors. Patient-related risk factors include: age, gender, weight (obesity), underlying diseases (i.e., diabetes, immunosuppression), etc. Procedure-related factors include patient skin preparation, duration of the procedure, surgical technique, OR personnel and air handling/ventilation, etc. Although there are overall general SSI risk factors, numerous studies have shown that there are also procedure-related risk factors (i.e., those specific for vascular vs cardiac vs orthopedic procedures).
- It is important to note that patient risk factors are not causes of infection because a patient cannot become infected without the pathogen. None of the patient-specific characteristics *causes* the infection. Such factors merely increase or decrease the risk of infection, if wound contamination occurs. The absolute requirement for PJI is contamination of the wound/implant. Without wound contamination, regardless of the patients' risk factors, they will not develop a PJI.

VI. Patient Warming and the Critical Importance of Infection Control in the Operating Room During Prosthetic Joint (Implant) Procedures

A. Patient Warming and Normothermia:

It has become common practice for surgeons to ensure normothermia in their patients. However, in my review of the literature in preparation of this report, I could find no clinical evidence supporting the hypothesis that ensuring normothermia reduces PJIs. Anesthesia, anxiety, antiseptic skin preparations, surgical irrigants, skin exposure, and large open surgical wounds in cold ORs can cause patients to become clinically hypothermic, defined as $<36^{\circ}\text{C}$, during surgery. Traditionally, hypothermia was thought of and used peri-operatively as a strategy to reduce cerebral and/or myocardial tissue sensitivity to ischemia. Hypothermia still is nearly universally used in cardiac surgery and selected other procedures. However, in the mid to

late 1990s, several studies suggested that inadvertent hypothermia during surgery could be associated with a variety of complications.

In evaluating the published literature on maintaining normothermia in surgical patients, several issues are important to understand. There are no standardized methods for when and how to measure patient temperature during surgical procedures. Even studies of the impact of hypothermia in surgical patients vary in the way (when and how) that core body temperature is measured. Sites that are accessible during surgery include the axillary, bladder, esophageal, nasopharynx, tympanic, and rectal sites. Some studies suggest that all these sites are not equivalent and accurate measures of core body temperature. The timing of core body temperature measurements also varies. Some measure continuously, some at the beginning and end of the surgical procedure, some before the incision and after return to the post-operative care unit, etc. The timing of these core body temperature measurements for comparative purposes is important. Thus, it is critical when reviewing the peer-reviewed literature to determine exactly how, when, and where the patient's core body temperature is being measured. In addition, virtually all surgical patients experience an initial drop in core body temperature associated with the induction of anesthesia in their first hour in the OR. One method to avoid or attenuate this initial response is to pre-warm surgical patients in the pre-operative area. Most studies of the impact of maintaining normothermia in surgical patients do not do this and so even patients who are being warmed in the OR experience this initial period of hypothermia. The impact of hypothermia (if any) also depends upon the actual change of delta in temperature and its duration. *Virtually no studies have evaluated the extent and duration of hypothermia on adverse events, including SSIs in PJI patients.*

One of the first studies to suggest that maintaining normothermia of surgical patients during the operative procedure was conducted by Kurz et. al (Kurz). In 1996, Kurz et al. conducted a randomized controlled trial (RCT) in which 200 colorectal surgery patients (actually specifically patients scheduled for an elective colorectal surgery for cancer or inflammatory bowel disease) were randomly assigned to routine intra-operative thermal care (i.e., the hypothermia group—core temperature allowed to decrease to approximately 34.5°C) or additional warming (i.e., the normothermia group—core temperature maintained near 36.5°C) using a FAW. The normothermia group also received warmed intravenous (IV) fluids whereas the hypothermia group did not. The authors concluded “that hypothermia itself may delay healing and predispose patients to wound infections. Maintaining normothermia intra-operatively is likely to decrease the incidence of infectious complications in patients undergoing colorectal resection and to shorten their hospitalizations.”

It should be noted that this is the only RCT to show a relationship between hypothermia and SSIs. Importantly, this study was only conducted in colorectal surgery patients. Some limitations of this study are: a) it was performed two decades ago when patient care was very different than today; b) the average duration of hospitalization at the time for such patients was 12-14 days vs. 5 days currently; c) in the hypothermia group, a FAW was used on ambient, so the ambient air (reported as 22°C) blowing on the patient may have had an additional cooling effect; d) most SSIs were superficial, not deep; e) the study was underpowered to detect a difference in deep SSIs; f) the average duration of the colorectal procedures was 3-4 hours vs. shorter periods today; g) patients received their “surgical prophylactic antimicrobial” for 3.5 days post-operatively; h) both patient groups experienced hypothermia, but the duration of hypothermia was greater in the hypothermia group; i) only 24 SSIs were detected (6 in the

normothermia and 18 in the hypothermia group); j) SSIs were significantly more common in smokers than non-smokers (23% vs. 7%); k) the normothermia group received warmed IV fluids whereas the hypothermia group did not; and l) the study was conducted in Vienna, Austria.

Dr. Kurz's deposition testimony acknowledges that this study's data are out of date, that this study probably would not be accepted for publication today, and that the surgical patients have much shorter durations of pre-operative hospital stay and are in better shape for surgery today than in 1996, and that even the surgical procedure itself is very different today than in 1996. In addition, she stated that the majority of SSIs were superficial and not deep SSIs. She also acknowledged that there are no other RCTs evaluating maintaining normothermia and the risk of SSIs (especially deep SSIs) in other surgical groups, particularly in shorter duration procedures such as PJA procedures. She stated that she had not done any studies of maintaining normothermia in PJA patients and she was not aware that anyone had assessed the relationship between normothermia/hypothermia and the risk of SSIs in PJA patients.

Shortly after the Kurz study, a variety of studies (mostly observational or retrospective studies not RCTs) found that maintaining normothermia did not impact SSI rates in a variety of surgical patient groups (Lehtinen, Wong, Barone, Constantine, Baucom, Melton, Kawaraguchi, Brown, and Frisch)

It is also undisputed that there is a wide variety of ways to try to maintain intra-operative normothermia other than the Bair Hugger FAW. These include: a) maintaining an OR temperature of $>24^{\circ}\text{C}$; b) using warming blankets, head coverings, and/or leggings; c) using warmed infusates/fluids; d) using warmed anesthetic gases; e) using heating mattresses, f) using reflective/conductive blankets; or g) using radiant heat sources. Moreover, several studies have shown that for longer procedures (i.e., >90 min) convective and conductive warming are equally efficacious (Brandt).

In summary, if one reviews the extensive peer-reviewed literature in this area and focuses on the data showing that maintaining normothermia in PJA patients will decrease their SSI risk (i.e., PJI), there are no well-designed RCTs to support this hypothesis. In fact, there are a variety of non-RCTs that suggest that maintaining normothermia vs. allowing inadvertent hypothermia has no impact on the SSI rate in PJA patients.

B. *Infection Control and Avoidance in Prosthetic Joint Arthroscopy (PJA) Procedures and Prosthetic Joint Infections (PJIs):*

PJAs, such as TKA or THA procedures, are a specific subset of all surgical procedures. PJA procedures are surgical procedures that involve a joint (i.e., elbow, shoulder, knee or hip replacement procedures). According to the CDC, in 2011, primary TKA procedures accounted for $>50\%$ of the 1.2 million PJA procedures (primary and revision) performed in the United States, followed by THAs (Berrios-Torres).

Contamination of the surgical field during PJA procedures can be catastrophic. In the United States, analysis of the Nationwide Inpatient Sample (NIS) using International Classification of Disease, ninth edition (ICD-9) data between 2001 and 2009 showed a significant increase in the risk of SSI following THAs or TKAs (THA: 1.99% to 2.18% and TKA: 2.05% to 2.18%,) (Kurtz, Jaekel). Between 1990 and 2004, the primary revision and knee arthroplasty infection rate rose from 0.63% to 1.21%. Between 1990 and 2004, the primary

revision and hip arthroplasty infection rate rose from 0.66% to 1.23%. By 2030, the SSI burden associated with THAs and TKAs is expected to increase to 6.5% and 6.8%, respectively. Given both the increasing SSI risk and the increasing number of individuals undergoing PJA, between 2010 and 2020, the total number of THA and TKA PJIs is projected to increase from 25,917 (THA: 8,136; TKA: 17,781) to 65,555 (THA: 16,584; TKA: 48,971).

As previously mentioned, the CDC's NHSN collects data for general risk factors for an SSI, but they do not collect procedure-specific (i.e., PJA) risk factors. Thus, the CDC risk index does not predict SSI risk very well for homogenous procedures—such as TKAs or THAs. In addition, the CDC NHSN has not required post-discharge surveillance. More recently, a large integrated healthcare system (IHCS) used a standard surveillance methodology for TKA and THA procedures from 1999 through 2004, including CDC definitions of SSI; however, they also included post-discharge SSI surveillance (not conducted by most of the CDC NHSN participants and not required by the CDC's NHSN)(Barnes). They compared their PJI rates to those reported by the CDC's NHSN. The IHCS infection rates (hip, 1.7; knee, 2.1) were higher than the corresponding CDC NHSN rates (hip, 1.4; knee, 1.2) (hip, $P = 0.006$; knee, $P = 0.012$) when infections detected by the IHCS during the post-discharge period were included.

Treatment of PJIs commonly involves a two-stage procedure, with 4-8 weeks of intravenous/parenteral antimicrobial therapy between the surgical procedures. When eradication of the PJI is not possible, treatment can include arthrodesis—surgical immobilization of the joint by fusion of the adjacent bones—or even amputation. In 2009, data from the NIS indicated that the average hospital cost for a revision of an infected THA or TKA was \$93,600 and \$24,200, respectively (Kurtz). Between 2001 and 2009, the estimated total hospital costs for treating PJIs increased from \$320 million to \$566 million, and was estimated to reach \$1 billion by 2014 (Kurtz, Jaekel, Cram). Examination of data from the U.S. Medicare population showed that between 1991 and 2010 TKA volume has increased from 93,230 procedures to 243,802 procedures (Cram). The TKA volume increase was driven by both the increased number of Medicare enrollees and the per capita utilization. Primary TKA utilization increased by 99% whereas revision TKAs increased by 51% over this twenty year period. Given the demographics of the U.S. population, it is reasonable to assume that the number of TKA and THA procedures will continue to increase over the next 1-2 decades.

In the OR it is impossible to remove the primary sources of contamination, i.e., the patient on whom the surgery is being performed and the essential OR staff. It follows that if one wishes to prevent the wound from becoming contaminated during the PJA procedure, it is necessary to interrupt the route of infection (Whyte 1988). Because PJA procedures are clean operations, the sources and the possible routes of infection are fewer than in many other operations. (Whyte 1988).

C. *How are the routes of infection managed and controlled in PJA surgeries?*

- To reduce the risk of PJIs associated with the OR environment and equipment, a number of interventions are implemented. Various pre-, peri-, and post-operative techniques have become standard to interrupt routes of infection.

- With regard to the patient, reducing the pre-operative hospital stay reduces the risk of colonization with hospital flora; pre-operative bathing and skin preparation reduces the normal skin flora; screening and decolonization of those colonized with *Staphylococcus* spp. reduces a source of PJI; and appropriate administration of prophylactic antimicrobials before the incision produces a peak of antimicrobial at the time of the incision and surgery are performed, thereby reducing the risk of surgical wound contaminating micro-organisms from causing an SSI.
- Keeping the OR doors closed and reducing/minimizing the number of surgical personnel in the OR and their frequency of OR entry/exiting reduces the microbial flora that these personnel disperse into the environment/air and reduce air from outside the OR from entering and mixing with OR filtered air.
- Ensuring appropriate sterilization of equipment, instruments, solutions, etc. having potential contact with the “sterile” surgical field reduces the risk of external contamination of the operative wound.
- Minimizing the equipment in the OR that is outside the operative field and ensuring that exhaust from such equipment does not impact the operative “sterile” field reduces the risk of contaminated air or fluids entering the operative field and contaminating the surgical wound.
- OR personnel practices to reduce the risk of SSI include appropriate pre-operative hand hygiene, wearing appropriate sterile personnel protective equipment (i.e., gowns, gloves, masks, hoods), and reducing the number and movement of OR personnel. These practices reduce the microbial burden on OR personnel, decrease the dispersal of OR personnel skin flora, and reduce surgical wound potential contamination in the OR. Additional practices include insuring good surgical technique, minimizing the duration of the procedure, and good hemostasis.
- The CDC and HICPAC have expressed strong concern about any air blowing devices in the OR and specifically have recommended “Nothing that blows air should be in an operating theater, if possible.” (CDC-A, B, and C).
- Ensure adequately filtered and circulated air in the OR. This may include either directional or non-directional air flow following HEPA filtration. A modern OR is designed to be supplied with “bacteria-free” (HEPA-filtered; removal of 99.97% of particles ≥ 0.3 microns) air of sufficient quantity to pressurize the room against the ingress of non-OR filtered air (i.e., the air is positive pressure compared to the area outside the OR). (Whyte 1988). Special handling (i.e., HEPA or other filtration) of the air entering the OR reduces the microbial flora in the air. In high risk PJA procedures, some even use directional or laminar air flow to further reduce microbial burden of air entering the operating room. Darouiche et al. have documented that using a device to capture potentially contaminated air near the incision site significantly reduces the particulates and CFUs and translates into reduced SSI rates (Darouiche).
- The main purpose of the above prevention interventions is to protect the surgical field and surgical wound from pathogens from the outlined primary and secondary reservoirs.

VII. The Relevance of Heater-Cooler Infections to Bair Hugger FAWs

- In 2013, Archermann et al. published a case report from Switzerland (Archermann). They noted that prosthetic valve endocarditis (PVE) due to slowly growing non-tuberculous mycobacteria (NTM) had not been reported previously. They presented one case of PVE and one case of bloodstream infection caused by *Mycobacterium chimaera* in 2012. Randomly-amplified polymorphic DNA (RAPD)-Polymerase chain reaction (PCR) indicated a relatedness of the two *M. chimaera* strains. Both patients had heart surgery two years apart from each other. **A nosocomial link was not detected.**
- Nearly two years later, Sax et al. described an outbreak of *M. chimaera* SSIs following cardiac surgery at a hospital in Switzerland (Sax). Based upon the Archermann et al. case report, they went back and reviewed microbiology records for patients with *M. chimaera* infections at their hospital. They identified six patients aged 49-64 years with PVE or vascular graft infection due to *M. chimaera*, which became clinically manifest with a latency of between 1.5 and 3.6 years after surgery. In addition, they cultured *M. chimaera* from water circuits of heater-cooler units (HCUs) connected to the cardiopulmonary bypass, and air samples collected when the units were in-use. RAPD-PCR demonstrated identical patterns among *M. chimaera* strains from HCU water circuits and HCU exhaust air samples, and strains in 2 patient clusters. They concluded that the epidemiological and microbiological features of this prolonged outbreak provided evidence for the airborne transmission of *M. chimaera* from **contaminated HCU water tanks to patients during open-heart surgery via exhaust air.**
- Over 250,000 procedures using cardiopulmonary bypass are performed in the United States each year. The implicated HCU devices represent approximately 60% of the U.S. market (Perkins). Yet, despite this large exposure, if it had not been for the fact that the infections were being caused by a very unusual organism, this link between *M. chimaera* infections and HCUs would not have been identified. HCUs had been used in cardiac surgery for decades to regulate patients' blood temperature during cardiopulmonary bypass. Yet, previously infected patients probably had not been cultured correctly for NTM (*M. chimaera*, a slow growing Mycobacteria, would not grow within 3 days which routine wound or blood cultures are incubated for growth).
- Once this link between HCUs and *M. chimaera* infections was established by Sax et al., others throughout the world began to look for these infections. *M. chimaera* infections (e.g., SSIs, endocarditis or bloodstream infections) have been detected and reported from a wide variety of countries around the world, including in the United States, Canada, Belgium, Germany, England, and Australia (Chand, Haller, Kohler, Perkins, Robinson, Sax, Soetaert, Sommerstein, and Trudzinski). None had recognized this association before the Sax et al publication. In some instances, the latency period between the surgery and signs of infection were as long as five years.
- An investigation at the manufacturing plant of one of the HCU devices showed that some of the devices were contaminated at the time of manufacture (intrinsic contamination). In other instances, the devices became contaminated during use (extrinsic contamination) (CDC-A, B, and C).

- Sax et al. also showed that the source of the infections in cardiac surgery patients was not from water used in the device (which has no contact with the patient), but rather was due to aerosolization of the exhaust air from the device. Infections in patients was because this contaminated exhaust circulated into the surgical field—no matter how far the devices were kept away from the operative field. This contamination of the surgical field even occurred when directional airflow was used in the OR. In fact, the only way to ensure that no contaminated air entered the sterile field was to keep the HCU (and its exhausted air) outside the OR in which the surgery was being performed (Sax).
- Only after intensive systematic investigation was the linkage between *M. chimaera* and HCU-associated infections in cardiac surgery patients identified. If one does not look for such a linkage (as was the case for decades as HCUs were used), the source of infections will not be found or recognized. This worldwide outbreak shows us that contaminated exhaust of a medical device used in the OR can lead to SSIs and other infections in surgical patients, even if all the prevention interventions mentioned previous are implemented. Furthermore, this outbreak illustrates that such devices can be used for long periods of time (decades) and unless the infections are caused by a very unusual organism and hospital personnel do the type of outbreak investigation we set as the gold standard, the source will remain unknown.
- The authors of several of the above studies concluded that: “all heater–cooler units should be reliably separated from air that can gain access to sterile areas and instruments, and devices that generate drafts should be banned from the operating room” (Sommerstein). The CDC’s HICPAC has stated at their November 2015 meeting that: “It is important not to blow air in the operating theater,” and adding, “Nothing that blows air should be in an operating theater, if possible.”(CDC-A). Furthermore, CDC has stated: “Had this infection been a more routine organism than *M. chimaera*, it may not have been attributed to the heater-cooler unit. Given the exhaust from these machines in the OR, it would not be surprising to learn that other organisms are aerosolized and deposited in places they do not belong.” Dr. Bell, Deputy Director, DHQP further stated: “the ultimate goals are to remove the problems, prevent them in the future, and hold industry accountable to develop safe products.”

The Bair Hugger FAWs are very, very similar to the HCUs. In fact, the Bair Hugger FAWs’ exhausted air is right next to the surgical field whereas the HCU exhaust was distant to the surgical field. Although they do not use water, the Bair Hugger FAWs draw in non-sterile OR air into their air intake. That air passes through (or around) an inadequate filter that has been shown to permit passage of micro-organisms into the device. Then, that air is heated in a device that has been shown to be internally contaminated. That heated air is then exhausted through a contaminated output hose into a blanket adjacent to the operative field. A blanket that has been shown to transfer soot from a burning device to the skin of a patient. Furthermore, if the contaminated air from the device does not reach the patient’s surgical field or wound directly, there is a second mechanism by which the Bair Hugger FAWs can cause serious infections. The excess or waste heat is released under the surgical field and through simple aerodynamics--as illustrated by Dr. Elghobashi’s excellent study--those convection currents rise and bring skin squames from the OR staff or other contaminants from the floor into the “sterile” surgical field. In my medical opinion, the mechanism of infection with the Bair Hugger FAWs is virtually identical to that documented with the HCUs.

VIII. The Consequences of Disruption in OR Ventilation for Joint Surgery Patients

Disruption of the air flow in the OR, such as that caused by the Bair Hugger FAW, increases particulates and microbial CFUs in the “sterile” surgical field. A variety of studies have demonstrated what the consequence is of increased particulates/CFUs in the “sterile” surgical field:

- Several studies have demonstrated a correlation between OR airborne bacterial contamination and post-operative PJIs (Gosden, Lidwell 1983, and Lidwell 1987).
- Stocks et al. showed that particulates are a reasonable proxy for airborne bioburden. They showed that there is a correlation between the particle count in the OR air and bacterial contamination (Stocks). In their study, they measured the number and size of airborne particles during 22 PJA procedures using an impact air sampler and settle plates. They found that the number of 10 micron particles/m³ and the number of surgical staff in the OR were associated with the CFU/m³ at the hip or knee joint surgical site. When they controlled for the number of 10 micron particles/m³, the number of surgical staff was not related to the CFU/m³. These data show that the number of particles and CFU increase together and that these particles can reach the surgical field. Traffic flows were not associated with higher particle counts (the OR was under 0.15 inches of water positive pressure). This study shows that particle counts may be an easier, quicker, and indirect but accurate method for detecting bacterial contamination of the OR air and surgical field.
- Darouiche et al. conducted an RCT testing the impact of an air barrier that reduced particulates and CFUs at the incision site and found: 1) that the CFU density at the incision site was significantly lower in the intervention group (i.e., air barrier) than in the control (P<0.001); 2) the density of airborne CFU at the incision site during the procedures were significantly related to the incidence of implant infection (P = 0.021); 3) that every 10 CFU/m³ increase in the median CFU density approximately doubled the probability of implant infection; 4) that airborne particle counts could be used as a proxy for ambient CFU; and 5) that airborne CFU densities were four times greater in the procedures with implant infections vs. no implant infection. All four implant infections occurred in the control group. The authors concluded that “reduction of airborne CFU specifically at the incision site during operations may be an effective strategy to reduce prosthetic-related infections” and that “airborne CFU entering incisions during operations is a likely source of contamination leading to implant infections.” This study demonstrated that particulate counts correlated with microbial counts (i.e., CFUs) and that elevated particulate counts/microbial counts at the incision site were associated with increased SSI risk and that by reducing the OR airborne particulate counts/CFUs at the incision site, the SSI rate was significantly reduced. (Darouiche).

For all these reasons, it is my expert opinion that equipment that blows hot air should not be permitted into ultra-clean surgical environments like those encountered in PJA surgeries because these devices significantly increase particulates and bacterial CFUs in the OR and thereby create an increased risk of infection for these patients. Furthermore, based on the report of Dr. Said Elghobashi’s detailed and impressive LES simulation analysis, together with the

published peer-review literature showing that the Bair Hugger FAWs increase particulates in the OR, it is my opinion, to a reasonable degree of medical certainty, that the Bair Hugger FAW more likely than not is a substantial contributing factor in the causation of PJIs.

In summary, having applied the methodological "gold standard" approach which I used in my work for the CDC, I have come to the conclusion that given the characteristics of Bair Hugger FAWs, that they more likely than not to a medical degree of certainty are associated with SSIs in PJA patients. The data to support this conclusion include: 1) particulate levels are correlated with microbial burden (i.e., CFUs) and both are correlated with SSI risk; 2) the Bair Hugger FAWs do not have HEPA filtration and have been found to be internally contaminated with pathogenic organism; 3) studies show that air can circumvent the filtration by passing around the filter; 4) the intake OR air is not sterile; 5) the intake hose, internal FAW device, exhaust or outtake hose have all been shown to commonly be contaminated at >90% levels with common skin organisms; 6) this contaminated air is exhausted in a blanket adjacent to the sterile surgical field; 7) the Bair Hugger FAW blanket has been shown to not be a "secondary filter" and has permitted soot from a burning FAW engine to exhaust soot onto a patient; and 7) the excess or waste heat from the Bair Hugger FAWs is released and causes convection currents under the operating table and thus would bring skin squames and other contaminants from the floor up and into the "sterile" surgical field. The data I have presented demonstrates that the Bair Hugger FAWs, to a reasonable degree of medical certainty, cause or substantially contribute to SSIs in PJA patients. For this reason, it is my opinion that the use of such devices should be abandoned or used only in low risk surgeries not involving implant patients.

I reserve the right to amend the opinions in this report, if further information becomes available to me.



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CDC-B, HICPAC Meeting, March 31, 2016: <https://www.cdc.gov/hicpac/pdf/mm/March-31-2016-HICPAC-Meeting-Summary-FINAL.pdf>

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Attachment B
Cases Testified as Expert at Trial or Deposition by William R. Jarvis, M.D.
(March 2013-March 2017)

Winston & Strawn LLP, Chicago, Illinois (SE Missouri Hospital and St. Francis Medical Center, on behalf of themselves and all others similarly situated v. C.R. Bard, Inc.). Deposition given.

Mr. Stephen M. Masters, Joliet, Illinois (Ronald Fuqua vs. Central Du Page Hospital Association). Deposition given.

Mrs. A. Candace Marcus, McIntosh Sawran Peltz & Cartaya, P.A., Fort Lauderdale, Florida (Bowman v. CCF Naples, et al.). Deposition given.

Mrs. Andrea Kott, Chicago, Illinois (Radak v. Evanston Northwestern Healthcare Corporation, et al.). Deposition given.

Mr. Mark Levine, Bartlit Beck Herman Palenchar & Scott LLP, Chicago, Illinois (ICU Medical, Inc. v. RyMed Technologies, Inc.). Deposition given.

Mr. Steven J Klearman, Reno, Nevada (Nolan v. South Lyon Health Center, et al.). Deposition given.

Mr. Thomas Saieva, Esq., Saieva & Stine, P.A., Tampa, Florida (Adolphson v Memorial Hospital of Tampa). Deposition given.

Mr. J. Dan Smith, McDonnell Boehnen Hulbert & Berghoff LLP, Chicago, Illinois (Ivera Medical Corporation v. Hospira, Inc.). Deposition given.

Mr. Ed Ciarimboli, Fellerman Ciarimboli Law, PC, Kingston, Pennsylvania (Una Valanski vs Hampton House, Hampton House Wilkes-Barre PA, LLC, HCR Manorcare, Leonard Kuchemba, M.D., Intermountain Medical Group). Trial testimony given.

Mrs. Carly S. Levin, Esq., Venable LLP, Washington, DC (Ivera Medical Corporation and Becton Dickinson and Company vs. Hospira, Inc. and Catheter Connections, Inc.). Deposition given.

Janet, Jenner & Suggs, LLC, Columbia, South Carolina (Frank Heaps, III v. Lexington County Health Services). Deposition given.

Mr. Ciarimboli, Fellerman Ciarimboli Law, PC, Kingston, Pennsylvania (Una Valanski vs Hampton House, Hampton House Wilkes-Barre PA, LLC, HCR Manorcare, Leonard Kuchemba, M.D., Intermountain Medical Group). Trial testimony given.

Mr. H. William McIntosh, The McIntosh Law Firm, PC, Kansas City, MO (Thurmond, et al. v. Kloster, et al.). Deposition given.

Mr. Ed Ciarimboli, Fellerman Ciarimboli Law, PC, Kingston, Pennsylvania (Janice Yalch vs. Alex Huang, M.D., J.T. Juang, M.D., P.C., Jung T. Huang, M.D., Geisinger South Wilkes-Barre Health System, Geisinger Clinic). Trial testimony given.

Mr. William W. Bird, The Bird Law Firm, P.C., St. Joseph, Missouri (James K. Sullwold, et al. v. Heartland Regional Medical Center a/k/a Mosaic Life Care, Inc.). Deposition and trial testimony given.

Mr. Theodore Walton, Clay Daniel Walton & Adams PLC, Louisville, Kentucky (Angie G. Huletter, Waller Hulette, Audrey Hulette, Emily Hulette and Andrew Hulette vs. GZA Geoenvironmental, Inc., et al.). Deposition given.

Mr. Jason C. Molesso, Sanders Viener Grossman, Mineola, New York (Loraine Angueira v. NYU Hospitals Center d/b/a NYU Hospital for Joint Diseases. Trial testimony given.

